

Disseminated histoplasmosis

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ABSTRACT

Disseminated histoplasmosis is a relentlessly progressive granulomatous disease which can mimic many other granulomatous diseases including tuberculosis. A 48-year-old male was referred to us with 11 months history of multiple subcutaneous swellings and ulcerations over the upper and lower limbs and fever for 2 months. He was evaluated outside for several months and received anti tubercular drugs for about 2 years in the past for a granulomatous infection of bone and soft tissue identified by various biopsies, without any improvement. When he was evaluated and fresh biopsies were taken, they were stained for fungus and disseminated histoplasmosis was detected. This case confirms the importance of considering fungal infections as a possibility while treating disseminated granulomatous infections, even in immune-competent patients, especially if response to treatment is inadequate.

Key words: Disseminated histoplasmosis, granulomatous disease, immune-competent

INTRODUCTION

Among the forms of histoplasmosis reported from India, disseminated histoplasmosis (DH) is the rarest. We report a case of DH in an immunocompetent individual treated initially with anti tubercular drugs for a granulomatous infection of bone and soft tissue with poor response from south India where the disease is uncommon. Clinical and laboratory features are similar to commonly seen granulomatous infections like tuberculosis. So by reporting this case we confirm the importance of considering disseminated fungal infections as a possibility while dealing with disseminated granulomatous infections in immunocompetent individuals although they come from a non-endemic area.

CASE REPORT

A 48-year-old rubber tapper came to our hospital with the symptoms of multiple subcutaneous swellings over upper

and lower limbs for 11 months and fever for 2 months. His past history revealed that he had a fall 13 years ago that resulted in a traumatic fracture of L2 vertebra and weakness in both lower limbs which was treated with spinal implant and he recovered uneventfully. However, 2 years ago he had a second fall that resulted in failure of the spinal implant. The implant was removed and the screw was left behind. A month later, he developed weakness of both lower limbs and a non-healing sinus at the surgical site. MRI of the spine taken that time showed a paraspinal collection [Figure 1]. Fine-needle aspiration cytology (FNAC) from this paraspinal collection showed granulomatous infection for which he received category I anti tubercular drugs for 13 months. However, at the end of this period, he was no better; also he developed swellings associated with ulceration over his right foot and left hand and fever for 1 month. Then the X-rays of foot and hand were taken which showed multiple periarticular lytic lesions [Figure 2]; open biopsy and curettage from these lesions showed granulomatous inflammation again. Hence, his treatment was changed to category II anti tubercular drugs which were continued for 9 more months. Although he was irregular for followup, he returned to the previous hospital at the end of ninth month of his cat II treatment because the swellings and ulcers had not healed in spite of the treatment, during which he was referred to our department of medicine from his previous hospital.

He gave no history of diabetes mellitus, hypertension, pulmonary tuberculosis, high risk behavior, intravenous drug abuse, blood transfusion, or of travel abroad. He was a heavy smoker of long standing, had loss of appetite and significant weight loss for 2 years. On examination, we found that he had ulcers over the left hand, right hand and right foot; generalized lymphadenopathy – firm, non-tender,

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Access this article online	
Quick Response Code:	Website: www.ijoonline.com
	DOI: 10.4103/0019-5413.121601

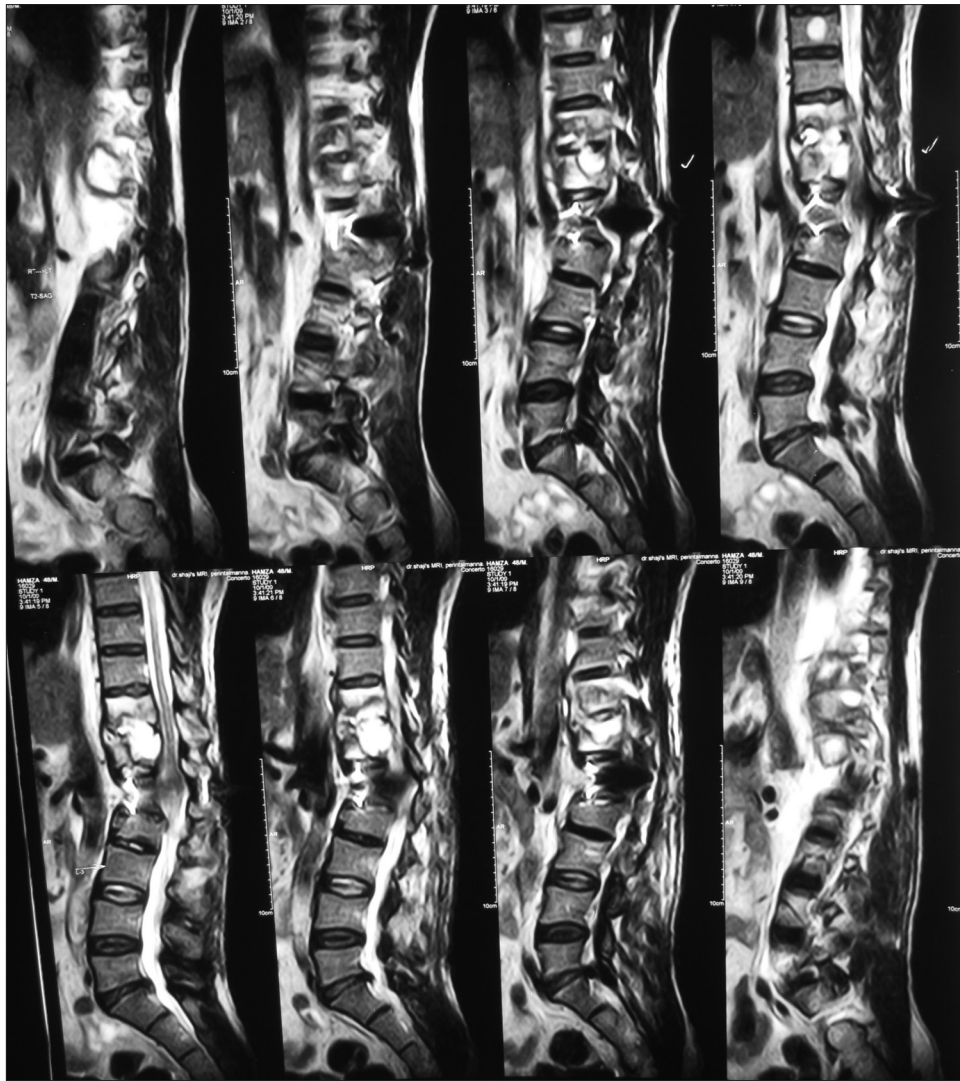


Figure 1: T2W MRI parasagittal and midsagittal images of spine showing paraspinal collection



Figure 2: X-ray of the feet (anteroposterior views) showing periarticular lytic lesions (white arrow)

mobile, painless with no matting or overlying sinuses; multiple subcutaneous swellings on the right forearm, right elbow and right leg; they were cystic, painless and mobile,

with a local rise in temperature; a surgical scar over the spine extending from T10 to L4 and a sinus at lumbar region.

His hemoglobin was 12.7 g/dL, total leukocyte count: 3400/L with 70% neutrophils, ESR: 45 mm/h and platelets: 2.3 lakhs/mm³. Peripheral smear showed normocytic normochromic anemia. Random blood sugar was 111 mg%. Liver and renal function tests were normal. The chest X-ray showed a non-homogenous opacity in the left upper lobe. HIV status was repeatedly negative. Ultrasonography of the abdomen revealed multiple enlarged intraabdominal lymph nodes. Blood culture was sterile.

Since the patient had evidence of a disseminated granulomatous disease from the previous histopathology reports, we considered atypical mycobacterial infection, fungal infection and sarcoidosis as possibilities. An excision biopsy of the cervical lymph node showed necrotizing granuloma [Figure 3]; the pathologist found on fungal staining capsulated yeast cells with narrow based budding

suggestive of histoplasma [Figure 4]. Fungal culture on Sabouraud's dextrose agar of pus from subcutaneous swelling showed growth of dimorphic fungus after 5 weeks of incubation, also consistent with histoplasma. A bone marrow biopsy showed granuloma [Figure 5].

Since the latest specimens showed histoplasma on fungal staining, the pathologist reviewed all previous slides of which the bone curettage specimen demonstrated the fungus Figure 5. Culture for atypical mycobacterium did not show any growth.

A diagnosis of DH was thus convincingly made. The patient was initially treated with liposomal amphotericin B for 14 days at a dose of 3 mg/kg followed by itraconazole 200 mg twice daily which was planned for the total of 12 months. So far he has received 8 months of treatment. Following this treatment his condition has improved. He became afebrile, his ulcers have healed, his swellings have subsided and his sinus has healed. He is on the followup with an impending treatment of itraconazole for the next 4 months.

DISCUSSION

Histoplasma capsulatum is a dimorphic fungus endemic to Ohio, Missouri and Mississippi River valleys in the United

States, as well as some river valleys in Central America.¹ Histoplasmosis may present clinically in different forms asymptomatic infection, an acute or chronic pulmonary infection, mediastinal fibrosis or granulomas and as DH. The development of progressive DH indicates impaired cell-mediated immune responses.² Patients who are immunosuppressed and unable to develop effective cell-mediated immunity against the organism are likely to manifest symptomatic disease during the period of acute dissemination.³

Chronic progressive DH is a slowly progressive infection due to *Histoplasma capsulatum* that occurs mostly in older adults who are not overtly immunosuppressed.⁴⁻⁶ These patients have no obvious immunosuppression, but their macrophages cannot effectively kill *H. capsulatum*.⁴ The symptoms of DH include fever, malaise, anorexia and weight loss. Physical examination often shows hepatosplenomegaly, lymphadenopathy, pallor and petechiae if pancytopenia is present and in some patients, mucous membrane ulcerations, skin ulcers, nodules, or molluscum-like papules.⁴⁻⁶ Progressive DH is treated beginning with lipid formulation amphotericin B (3-5 mg/kg/d or amphotericin B (0.7-1.0 mg/kg/d for 1-2 wk), then itraconazole (200 mg twice daily for 12 mo).⁷

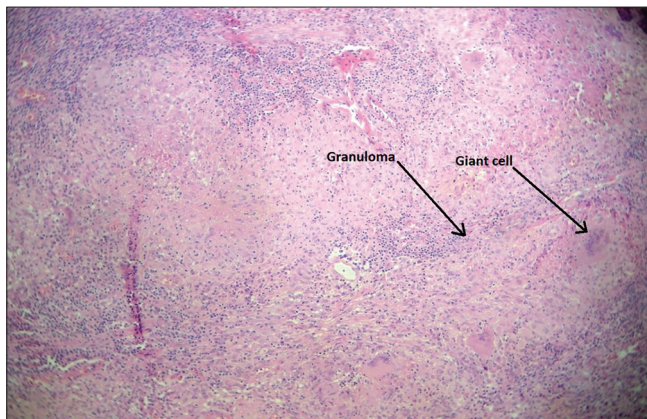


Figure 3: 10x micrograph of a lymph node biopsy showing necrotizing granuloma with hematoxylin and eosin staining

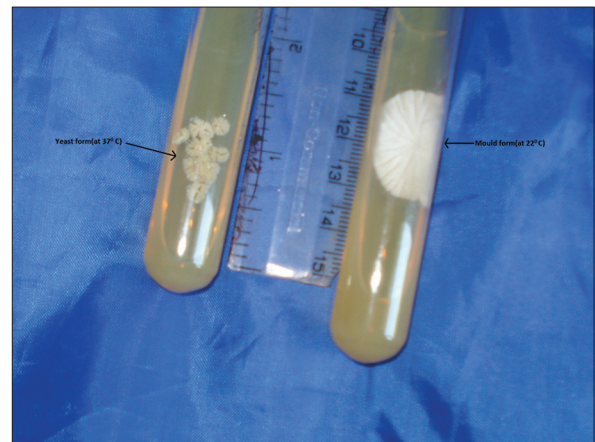


Figure 4: Fungal culture on Sabouraud's dextrose agar

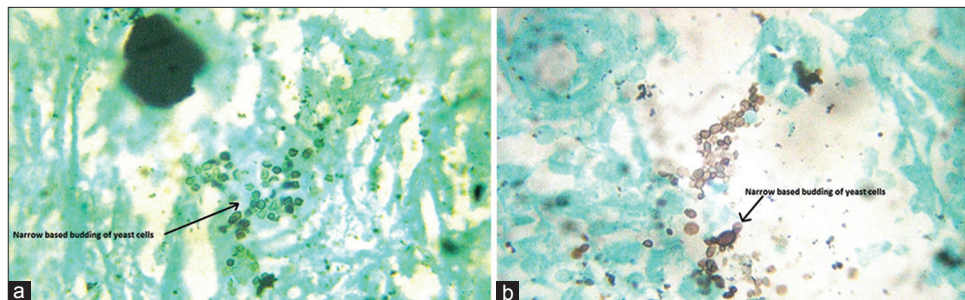


Figure 5: 40x micrograph of (a) a lymph node biopsy showing histoplasma with Gomori's methenamine silver staining (b) a biopsy ulcer on fifth toe showing histoplasma with Gomori's methenamine silver staining (black arrow)

In India, histoplasmosis seems to be prevalent in the Gangetic delta.⁸ Panja and Sen reported the first case of DH from Calcutta in 1954.⁹ Among the forms of histoplasmosis reported from India, DH is the rarest. Numerous case series have reported histoplasmosis from all over India, the largest series being from Delhi, a compilation of 37 patients from all over India.¹⁰ There are sporadic reports from Andhra Pradesh and Bihar as well.² Since clinical and laboratory features have considerable overlap, it is important to consider fungal infections while dealing with disseminated granulomatous infections although patient is immunocompetent.

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How to cite this article: Mansoor CA, Bhargavan PV, Rajanish R, Nair LR. Disseminated histoplasmosis. *Indian J Orthop* 2013;47:639-42.

Source of Support: Nil, **Conflict of Interest:** None.